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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/396,985	09/15/1999	BRUCE A. BEUTLER	UTSD:602	8202

7590

04/23/2002

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EXAMINER

BASI, NIRMAL SINGH

ART UNIT	PAPER NUMBER
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1646

DATE MAILED: 04/23/2002

16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/396,985

Applicant(s)
BEUTLER ET AL

Examiner
Nirmal S. Basi

Art Unit
1646



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Aug 14, 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 38-40, 52-61, 63-68, 70-75, and 100-103 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 38-40, 52-61, 63-68, 70-75, and 100-103 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

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DETAILED ACTION

1. Amendment filed 1/22/02, paper number 15 has been entered.

Response To Applicants arguments

2. Claims 38-40, 52-61, 63-68, 70-75 and 100 remain rejected under 35 U.S.C. 112, second paragraph, for reason of record in paper number 14, 8/14/01, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 38, 40 and 52 remain indefinite because the name TLR-4 has not been defined in the claims and specification so as to allow the metes and bounds of the claims to be determined.

Applicant argues TLR-4 has been defined to meet the requirements of 35 USC 112, second

paragraph. Applicant argues the name TLR-4 is defined in the specification and is well known and defined in the literature. Applicants arguments have been fully considered but not found persuasive.

The art nor specification disclose the structural and functional properties which must be present for the polypeptide to be classified as a TLR-4 polypeptide. The name TLR-4 polypeptide encompasses,

in view of the specification, modifications and changes which may be made to TLR-4 protein and subunits and still obtain a molecule having like or otherwise desirable characteristics ,see page 73.

The structure associated with polypeptide encompassed by the name and the "like or otherwise desirable characteristics" are not disclosed so as to allow the metes and bounds of the claim to be determined. Applicants states on page 6, of paper number 11, filed 2/7/01, that the name has already been changed once from Toll-4 to TLR-4. Similarly other proteins may have different names, but

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encompass the same protein. Therefore without a clear disclosure of the structure and associated function of the TLR-4 protein the metes and bounds of the claim cannot be determined.

In response to the rejection of claims 38 and 52 Applicant argues a description of the events and circumstances that comprise the initiation of a response to LPS and the resultant response are disclosed in the specification, further Applicant states exemplary parameters and methods for measuring and determining the response are also found in several locations in the specification. Applicants arguments have been fully considered but not found persuasive. The specification does not provide a clear definition of the “lipopolysaccharide mediated response” and therefore the parameters used to determine the response can not be determined. The “lipopolysaccharide mediated response” and the parameters screened to determine the response are not defined so as to allow the metes and bounds of the claim to be determined. Where does the “lipopolysaccharide pathway” begin and end so the metes and bounds of the “lipopolysaccharide mediated response” can be determined?

Claim Rejection, 35 U.S.C. 112, second paragraph

3. Claims 38-40, 52-61, 63-68, 70-75 and 100-103 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Amended claim 52 and newly added claims 101-103 are indefinite because it is not clear what is encompassed by "mediation of the liposaccharide mediated response" so as to allow the metes and bounds of the claim to be determined.

5 Amended claims 38, 40 and 52 are indefinite because it is not clear what is encompassed by "liposaccharide mediated response", for the reasons given above, so as to allow the metes and bounds of the claim to be determined.

Claims 38, 40, 52, 55, 56 and 63-64 are indefinite because it is not clear what is a TLR-4. "TLR-4" is indefinite for reasons given above.

10 New claims 101-103 is indefinite because it is not clear what is a, "small molecule", so as to allow the metes and bounds of the claim to be determined. The term "small molecule" in claims 101-103 is a relative term which renders the claim indefinite. The term "small molecule" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. When is molecule considered small as compared to when it is considered big so as to
15 allow the metes and bounds of the claim to be determined. Also what is the boundary when a molecules transitions into a medium or big molecule?

Claim 71-73 are is indefinite because "stimulator of an immune response" does not provide any structural limitations to the modulator or the metes and bounds of the immune response.

20 Claims 39, 53-54, 57-61, 65, 66, 68, 70, 74-75 are indefinite for depending on a base claim or intermediate claim and fail to resolve the issues raised above.

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Applicants arguments have been fully considered regarding the rejections of the above claims under 35 U.S.C. 112, second paragraph, but not found persuasive for the reasons given above.

Claim Rejection, 35 U.S.C. 112

5 4. Amended claims 38, 40, and 52, original claims 38-40, 52-61, 63-68, 70-75 and newly added
claims 100-103 are rejected under 35 U.S.C. 112, first paragraph, for reasons of record in paper
number 14, 8/14/8, because the specification, while being enabling for a screening method for
compounds which modulate a LPS mediated response by inducing the synthesis or altering
expression of TLR-4 of SEQ ID NOs: 2, 4, 6, 98 and 99, does not reasonably provide enablement
10 for other methods of screening for compounds which may affect any other LPS-mediated responses
or methods for identification of compounds which may predictably have other activities by any way
other means than the altered expression of TLR-4 (SEQ ID Nos:2, 4, 6, 98 and 99). The,
specification does not enable any person skilled in the art to which it pertains, or with which it is
most nearly connected, to make and use the invention commensurate in scope with these claims.
15 Applicants arguments have been fully considered but not found persuasive for the reasons given
below.

Applicant argues LPS response disclosed by the specification is by far not the sole means of
modulating the TLR-4 response. Applicant further states signaling in the TLR-4 pathway results
for example in an increase Tnf production as a result of liposaccharide contact with cell surface
20 receptors. Applicants arguments have been considered but not found persuasive.

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The claims are directed to screening for modulators of a LPS mediated response. The specification discloses that TLR-4 mRNA is induced by LPS (Fig 9) and TLR4 is the limiting factor in LPS signal transduction in LPS responsive macrophages, the quantity of TLR4 expressed is an important limiting factor in the intensity of the signal that is evoked (page 128). The specification discloses the screening of modulators of LPS mediated response where the compounds screened can modulate the expression of TLR-4 of SEQ ID NOs:2, 4, 6, 98 and 99. The scope of the claims which encompasses other methods of screening for modulators of LPS, using proteins other than those disclosed in SEQ ID NOs:2, 4, 6, 98 and 99, where the compounds may have activity by other means than the altered expression of TLR-4 expression of SEQ ID NOs:2, 4, 6, 98 and 99 is not enabled by the disclosure. For the person of ordinary skill in the art to screen for modulators of a LPS mediated response by any other means than those disclosed as “enabling” above, the artisan must first isolate other proteins capable of direct or indirect interaction with LPS and its modulators, and develop screening assays to determine if certain compounds can be modulators of the LPS mediated response. Therefore, the lack of guidance provided in the specification as to what other assays may be used to screen for modulators of LPS (see rejection under 112, second paragraph disclosing the difficulty in determining what is the scope of the liposaccharide mediated response), unpredictability and undue experimentation in isolating other TLR-4 polypeptides would prevent the skilled artisan from practicing the invention in its full scope.

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No claim is allowed

Advisory Information


Any inquiry concerning this communication or earlier communications from the examiner
5 should be directed to Nirmal Basi whose telephone number is (703) 308-9435. The examiner can
normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor,
Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703)
10 308-0294.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal
communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding
15 should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nirmal S. Basi
Art Unit 1646
April 22, 2001

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YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600